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Application of:	Palese, et al	Confirmation No.:	4644
Serial No.:	09/070,629	Art Unit:	1648
Filed:	April 30, 1998	Examiner:	Scheiner, L.
For:	RECOMBINANT INFLUENZA VIRUSES EXPRESSING TUMOR-ASSOCIATED ANTIGENS AS ANTITUMOR AGENTS	Attorney Docket No:	6923-071-999

DECLARATION OF DR. ADOLFO GARCIA-SASTRE UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, ADOLFO GARCIA-SASTRE, do declare that:

1. I am a co-inventor of the above-identified application relating to recombinant influenza viruses comprising a heterologous sequence which encodes a tumor antigen within the influenza viral genome and vaccine formulations thereof.

2. I am an Assistant Professor of Microbiology at the Mount Sinai School of Medicine, the assignee of the above-identified patent application. I have extensive experience in the field of negative strand RNA viruses, in particular, influenza virus, and methods for engineering recombinant virus, in particular, for the purpose of designing vaccines, as evidenced by my curriculum vitae, attached hereto as Exhibit A.

3. The invention described in the above-identified application relates to recombinant influenza viruses that have been engineered to express tumor antigens and their use to "immunize" hosts in order to generate an immune response that leads to tumor regression or to prevent tumor formation. The invention is based, in part, on the discovery that the recombinant influenza viruses of the invention induce a potent and specific cell-

mediated immune response against the expressed antigen. In accordance with the invention, the recombinant influenza viruses may be engineered to express a variety of tumor antigens, including gp100, MART-1/Melan A, TRP-1, Tyrosinase, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, N-acetylglucosaminyltransferase, p15, beta-catenin, MUM-1, CDK4, Her-2/neu, human papilloma virus E6 or E7, or Muc-1.

4. The following analyses was carried out by me personally, or under my direction or supervision, using the teachings of the above-identified application to construct a recombinant influenza virus which expresses a tumor antigen, the HER-2 E75 epitope, derived from human HER-2/neu protein, and to determine that the recombinant influenza virus so constructed does elicit a potent and specific immune response against the expressed antigen. The results of this study reveal that such a recombinant influenza virus does elicit significant cytotoxic T lymphocyte (CTL) response against the expressed antigen and against tumors expressing the specific antigen (E75 antigen).

5. In order to construct the recombinant influenza virus, an attenuated form of influenza A/PR8/34 was used as a viral vector. This attenuated virus (KIF-NS virus) was engineered to express a tumor antigen, E75 (KIF), derived from the human HER-2/neu protooncogene. The virus was constructed using standard techniques, such as those described in the specification of the instant application (see, e.g., the instant specification at page 8, line 31 to page 10, line 29, or page 17, lines 3 to 36), to generate recombinant influenza virus expressing a tumor antigen. Expression plasmids containing cDNAs for PR8 viral genes were modified as follows: to construct an attenuated virus, mutations causing single amino acid alterations were introduced into the PB2, PA, and NP genes, and stop codons were inserted into the NS gene to truncate the NS1 protein. For tumor antigen expression, amino acids 65-71 of the viral neuraminadase (NA) protein were modified to substitute amino acids KIFGSLAFL, the E75 epitope of the HER-2 gene product. These plasmids were introduced into cultured cells by transfection of mixed 293-T cells and MDCK cells with plasmid DNAs corresponding to the viral genes. Following amplification in embryonated chicken eggs, recombinant virus was isolated and viral identities confirmed by RT-PCR and restriction/sequence analysis.

6. The recombinant influenza virus expressing a tumor antigen ("KIF-NS containing E75 virus") was tested for its ability to elicit a cell based immune response. In

particular, the KIF-NS containing E75 virus was assayed for:

(1) its ability to infect immune cells, e.g., immature dendritic cells;

(2) its ability to activate cellular immunity, e.g., induce IFN-gamma (IFN-γ);

(3) its ability to activate cellular immunity specific to the tumor antigen; and

(4) its ability to induce lysis of tumor cells expressing the specific tumor antigen.

7. The ability of the recombinant virus expressing a tumor antigen to induce an immune response was determined using standard assays and techniques, such as those described in the instant application (see, e.g., the instant specification at page 20, line 34 to page 21, line 12). The ability of the KIF-NS containing E75 virus to infect immune cells, e.g., dendritic cells (DCs), and subsequently induce expression of NA on the surface of DCs was analyzed. DCs present foreign antigens to CTLs and induce CTL response to the antigen, so antigen expression on DCs is an early step in the stimulation of CTL cytotoxic activity. DCs were incubated with KIF-NS containing E75 virus in culture. Following incubation, cells were washed, stained with antibodies to NA protein, and analyzed by flow cytometry. The results of this assay showed that both immature and LPS-stimulated DCs can be infected by KIF-NS virus and can present recombinant viral antigens on their cell surfaces. This indicates that the KIF-NS containing E75 virus is able to infect immune cells and initiate the first steps of the CTL immune response.

8. The ability of the KIF-NS containing E75 virus to activate cellular immunity as measured by induction of IFN-γ was examined. In an immune response, T cells specific to a presented epitope are activated following antigen presentation, resulting in induction of IFN-γ. To determine whether the KIF-NS virus containing E75 can induce an IFN-γ response specific to the E75 epitope, tumor-associated lymphocyte T-cells (TALs) primed with KIF-NS containing E75 virus infected DCs were restimulated by exposure to DCs presenting either the tumor antigen E75, or control peptides. In response to DCs presenting E75 peptide, TALs secreted four times greater levels of IFN-γ than seen in response to control DCs. This demonstrates that the KIF-NS containing E75 virus-infected DCs can activate E75-specific T cells to secrete IFN-γ as part of the cellular immune response.

9. The ability of the KIF-NS containing E75 virus to activate cellular immunity specific to the tumor antigen, the E75 epitope, was assayed. "Effector" CTLs, characterized by the presence of CD45RO markers and a lack of CCR7 markers, and "central memory" CTLs, characterized by the presence of both CD45RO and CCR7 markers, are components of a CTL-mediated immune response. To determine if priming with KIF-NS containing E75 virus infected DCs leads to expansion of effector and central memory CTLs, peripheral blood mononuclear cells (PBMCs) were stimulated with DCs infected with KIF-NS containing E75 virus, and the presence of $E75^{+}$-CTLs was determined by flow cytometry. Compared to control PBMCs stimulated with uninfected DCs, PBMCs primed with KIF-NS containing E75 virus infected DCs showed a greater percentage of $E75^{+}$-CTLs in the total T cell population. Analysis of CCR7 and CD45RO markers revealed that priming of PBMCs with KIF-NS infected DCs leads to expansion of both effector and memory CTLs, an indication of activation of E75-specific T cells.

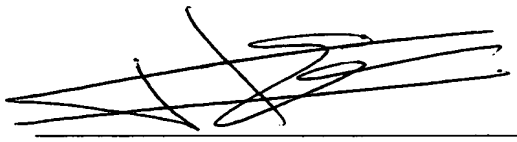
10. The ability of the KIF-NS containing E75 virus to induce lysis of tumor cells expressing the E75 antigen was studied. TALs primed with KIF-NS virus-infected DCs showed specific lysis of T2 T cells exposed to E75 ("E75-pulsed T2 cells"), indicating activation of E75 tumor-specific cytotoxic T lymphocytes (CTLs). The results of this assay were expanded by a second assay examining the ability of primed CTLs to preferentially recognize E75 antigen presented by tumor cells. Tumor lysis experiments were performed using as a target radiolabeled tumor cells from the tumor cell line SKOV3.A2 in the absence or presence of unlabeled target inhibitor T2 cells (unlabeled E75-pulsed T2 cells). In the presence of E75-pulsed T2 cells, CTLs that recognize E75 will show preferential lytic activity toward the T2 cells, resulting in a decrease in lysis of the labeled SKOV3.A2 cells. A population of TALs primed with KIF-NS containing E75 virus-infected DCs showed inhibition of SKOV3.A2 cell lysis in an E75-specific manner. Re-stimulation of TALs by KIF-NS containing E75 virus-infected DCs enhanced this inhibitory effect, suggesting that tumor-reactive E75-specific T cells expanded at re-stimulation. These results indicate that the KIF-NS containing E75 virus can induce lysis of tumor cells expressing the E75 tumor antigen.

11. In summary, these analyses indicate that a recombinant influenza virus expressing a tumor antigen, KIF-NS, containing the HER-2 E75 virus, may be engineered following the teaching provided in the specification of the instant application. Further, these

analyses further indicate that the ability of said virus to induce a cellular immune response and an immune response specific to tumor cells expressing the tumor antigen may be determined using standard assays as provided in the specification of the instant application. The recombinant influenza virus expressing a tumor antigen, the E75 antigen, was shown to induce both a cellular immune response and an immune response specific to tumor cells expressing the tumor antigen, thus demonstrating the efficacy of said recombinant virus as a tumor vaccine.

12. I declare further that all statements made in this Declaration of my own knowledge are true, and that all statements made on information and belief are believed to be true, and further, that these statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: July 14, 2003



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CURRICULUM VITAE

1.- PERSONAL INFORMATION

NAME: **Adolfo GARCIA-SASTRE.** SEX: Male.

DATE & PLACE OF BIRTH: October 10, 1964; Burgos, Spain.

CITIZENSHIP: Spain.

IMMIGRANT STATUS: American permanent resident

SOCIAL SECURITY NUMBER: 082-82-2444

MARITAL STATUS: Married

HOME ADDRESS: 16 E 96 St, Apt 3G.
New York, NY 10128, USA.
Phone #: 212-2894262.

OFFICE ADDRESS: Department of Microbiology, Mount Sinai School of Medicine, Box 1124.
1 Gustave L. Levy Place, New York. 10029 NY, USA.
Phone #: 212-2417769.
Fax #: 212-5341684.
E-mail: adolfo.garcia-sastre@mssm.edu

2.- EDUCATION

-**Bachelor** in Biological Sciences, Faculty of Biology, University of Salamanca, Spain. 1986.
Mark obtained: "Sobresaliente" (highest possible mark in Spain).

-**Master** in Biochemistry, Faculty of Biology, University of Salamanca, Spain. 1986.
Mark obtained: "Sobresaliente" (highest possible mark in Spain).

-**Ph.D.** in Biochemistry and Molecular Biology, Faculty of Biology, University of Salamanca, Spain. 1990.
Mark obtained: "Sobresaliente cum laude".

-**Post doctoral fellow** in Microbiology, Mount Sinai School of Medicine, New York, USA. 1991-1994.

3.-**RESEARCH EXPERIENCE**

-**Research Fellow**, Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Salamanca, Spain. January 1987 to December 1990. **Topic**: Structure and function of Newcastle Disease Virus.

-**Research Fellow**, Unité d'Ecologie Virale, Institut Pasteur, Paris, France, November 1987 - December 1987. **Topic**: Immunological characterization of Influenza A and B viruses.

-**Research Fellow**, Unité d'Ecologie Virale, Institut Pasteur, Paris, France, April 1989. **Topic**: Serology of Influenza C virus in men and dogs.

-**Postdoctoral Research Fellow**, Department of Microbiology, Mount Sinai School of Medicine, New York, USA. February 1991 to December 1994. **Topic**: Genetic manipulation of influenza viruses.

-**Research Assistant Professor**, Department of Microbiology, Mount Sinai School of Medicine, New York, USA. January 1995 to December 1996.

-**Assistant Professor**, Department of Biochemistry and Molecular Biology, School of Medicine, University of Salamanca, Salamanca, Spain. March 1995 to February 1997.

-**Assistant Professor**, Department of Microbiology, Mount Sinai School of Medicine, New York, USA. January 1997 to July 2001.

-**Associate Professor,** Department of Microbiology, Mount Sinai School of Medicine, New York, USA. July 2001 to present.

4.-**AWARDS, FELLOWSHIPS AND GRANTS**

-**Research Fellowship** from the Spanish Ministry of Education and Science. January 1987 to December 1990.

-**Research Fellowship** from the French Foreign Office, November 1987 - December 1987.

-**Research Fellowship** from the French Foreign Office, April 1989.

-Spanish "Royal Academy of Pharmacy" **Research Awardee**, December 1986.

-**Master Awardee**, University of Salamanca, Spain, 1986.

-**Bachelor National Awardee** from the Spanish Ministry of Education and Science, 1986.

-**Study Fellowship** from the University Menéndez Pelayo, Santander, Spain, September 1987.

-**Ph.D. Fellowship** from the "Caja de Ahorros Municipal de Burgos", February 1991.

-**Ph.D. Awardee**, University of Salamanca, Spain, 1992.

-**Research Fellowship** from NATO, December 1991 to March 1993.

-**Research Fellowship** from the Spanish Ministry of Education and Science (**Fulbright**). April 1993 to December 1994.

-**Grant-in-aid** from the Stony Wold-Herbert Fund, Inc., New York, July 1995 to June 1997. Project: "Expression of foreign antigens by influenza virus vectors".

-**PI of R29 research grant** from NCI/NIH, (1R29CA77432-01), April 1998 to March 2003. Project: "Transfectant influenza viruses in cancer therapy"

-**PI of AMFAR research grant** (02621-26-RGV), May 1999 to April 2000. Project: "Novel vaccines based on Newcastle disease virus vectors"

-**PI of R01 research grant** from NIAID/NIH (1R01AI46954-01A1), July 2000 to June 2005. Project: "Virulence factors of influenza virus: The NS1 protein"

-**CoPI of subproject of the P01 research grant** from NIAID/NIH (1P01AI 48204-01), July 2000 to June 2004. PI: Peter Palese. Project: "Immunogenicity of recombinant human influenza A and B viruses"

-**Collaborator of subcontract of the UC1 challenge grant** from NIAID/NIH (1UC1AI49519), October 2000 to September 2003, PI: Dennis Trent. Project: "DNA based generation of avian influenza virus vaccines"

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2.- A. GARCÍA-SASTRE, J. A. CABEZAS & E. VILLAR: Proteins of Newcastle disease virus envelope: interaction between the outer hemagglutinin-neuraminidase glycoprotein and the inner non-glycosylated matrix protein.
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45.- N. DONELAN & A. GARCÍA-SASTRE: Inhibition of the 2-5A synthetase activity by the NS1 of influenza A virus.
19th Annual Meeting of the American Society for Virology. Fort Collins, Colorado, USA. July 2000.

46.- A. GARCÍA-SASTRE: NS1-mediated inhibition of the type I interferon system during influenza a virus infection.
Options for the Control of Influenza IV. Hersonissos, Crete, Greece. September 2000.
Chair of the session Structure-function relationship.

47.- H. ZHENG, N. P. RESTIFO & A. GARCÍA-SASTRE: Therapeutic properties in mice of a transfectant influenza A virus expressing a tumor associated antigen model.
Options for the Control of Influenza IV. Hersonissos, Crete, Greece. September 2000.

48.- C. F. BASLER, J. K. DYBING, T. A. JANCEWSKI, H. ZHENG, M. SALVATORE, A. H. REID, M. L. PERDUE, A. GARCÍA-SASTRE, P. PALESE & J. K. TAUBENBERGER: Characterization of transfectant influenza viruses bearing the NS gene of the 1918 influenza virus.
Options for the Control of Influenza IV. Hersonissos, Crete, Greece. September 2000.

49.- A. GARCÍA-SASTRE: Molecular mechanisms for influenza virus attenuation and vaccine development.
International Symposium on Emergence and Control of Zoonotic Ortho- and Paramyxovirus

Diseases. Les Pensières, Veyrier-du-Lac, France. December 2000.

50.- M. SALVATORE, C. F. BASLER, S. BOURMAKINA, P. PALESE & A. GARCÍA-SASTRE: Effects of influenza A virus NS1 protein on cellular and viral protein expression. 20th Annual Meeting of the American Society for Virology. Madison, Wisconsin, USA. July 2001.

51.- J. SCHICKLI, A. FLANDORFER, A. GARCÍA-SASTRE & P. PALESE: Rapid generation of high yield H1N1 and H3N2 influenza A viruses by a plasmid-only system. 20th Annual Meeting of the American Society for Virology. Madison, Wisconsin, USA. July 2001.

52.- C. F. BASLER, F. ABAITUA, J. R. RODRUÍGUEZ, H. ZHENG, M. ESTEBAN, P. PALESE & A. GARCÍA-SASTRE: Phenotypic rescue of an NS1 knock-out influenza virus and of an E3L knock-out vaccinia virus by expression in trans of E3L or NS1 proteins. Annual Meeting of the International Society for Interferon and Cytokine Research ISICR. Cleveland, Ohio, USA. October 2001.

53.- X. WANG & A. GARCÍA-SASTRE: Functional replacement of the carboxy terminal domain of the NS1 protein of influenza a virus by heterologous dimerization domains. Research Conference on Orthomyxoviruses. Texel, The Netherlands. November 2001.

54.- J. CROS, T. NAKAYA, M. S. PARK, Y. NAKAYA, H. ZHENG, A. SAGRERA, E. VILLAR, A. GARCÍA-SASTRE & P. PALESE: Recombinant Newcastle disease virus as a vaccine vector against influenza viruses. Research Conference on Orthomyxoviruses. Texel, The Netherlands. November 2001.

55.- S. BOURMAKINA & A. GARCÍA-SASTRE: Genetic determinants of influenza A virus filamentous morphology. 21st Annual Meeting of the American Society for Virology. Lexington, Kentucky, USA. July 2002.

56.- T. M. TUMPEY, A. MIKULASOVA, A. GARCÍA-SASTRE, J. K. TAUBENBERGER, D. E. SWAYNE, P. PALESE & C. F. BASLER: Would the 1918 pandemic influenza virus pose a threat today? 21st Annual Meeting of the American Society for Virology. Lexington, Kentucky, USA. July 2002.

57.- A. MIKULASOVA, L. MARTINEZ-SOBRIDO, A. GARCÍA-SASTRE, P. PALESE & C. F. BASLER: The Ebola virus VP35 protein blocks type I interferon production by preventing activation of IRF-3. 21st Annual Meeting of the American Society for Virology. Lexington, Kentucky, USA. July 2002.

58.- A. GARCÍA-SASTRE & X. WANG: Functional substitution of the carboxy terminal domain of the NS1 protein on influenza A virus by heterologous dimerization domains. XIIth International Congress of Virology. Paris, France. July 2002.

59.- S. LUDWIG, X. WANG, C. EHRHARDT, H. ZHENG, O. PLANZ, S. PLESCHKA, A. GARCÍA-SASTRE & T. WOLFF: The influenza virus NS1 protein inhibits activation of Jun-N-terminal kinase (JNK) and AP-1 transcription factors.
XIIth International Congress of Virology. Paris, France. July 2002.

59.- N. DONELAN, C. F. BASLER & A. GARCÍA-SASTRE: Role of the dsRNA-binding activity of the NS1 protein of influenza A virus in its type I interferon antagonist properties. Annual Meeting of the International Society for Interferon and Cytokine Research ISICR 2002. Turin (Italy). October 2002.

60.- A. GARCÍA-SASTRE, M-S. PARK, L. MARTINEZ, J. MUÑOZ, M. SHAW, J. CROS, T. NAKAYA, N. BOUVIER & C. F. BASLER: Identification of type I interferon antagonists using recombinant Newcastle disease virus.
Annual Meeting of the International Society for Interferon and Cytokine Research ISICR 2002. Turin (Italy). October 2002.

61. - A. FERNANDEZ-SESMA, A. GARCÍA-SASTRE & T. MORAN: Immunization with an influenza virus lacking the NS1 protein confers protection in mice against a heterosubtypic virus challenge.
Annual Meeting of the International Society for Interferon and Cytokine Research ISICR 2002. Turin (Italy). October 2002.

62.- A. GARCÍA-SASTRE: Plasmid-based reverse genetics for influenza virus.
Workshop on Engineering RNA Virus Genomes as Biosafe Vectors. Madrid (Spain). October 2002.

63.- T. NAKAYA, J. CROS, M.-S. PARK, Y. NAKAYA, H. ZHENG, A. SAGRERA, E. VILLAR, A. GARCÍA-SASTRE & P. PALESE: Recombinant Newcastle disease virus (NDV)
Workshop on Engineering RNA Virus Genomes as Biosafe Vectors. Madrid (Spain). October 2002.

63.- M. HUARTE, A. FALCÓN, Y. NAKAYA, J. ORTÍN, A. GARCÍA-SASTRE & A. NIETO: Functional studies of PA subunit of influenza virus polymerase using rescued viruses
Workshop on Engineering RNA Virus Genomes as Biosafe Vectors. Madrid (Spain). October 2002.

5.3. EDITOR

1.- P. PALESE & A. GARCÍA-SASTRE, eds. "The future of vaccine design." Perspective

series of The Journal of Clinical Investigation, 2002.

6.- **MEMBERSHIPS**:

1.- Member of the American Society for Microbiology since 1993.

2.- Member of the International Society for Vaccines since 1995.

3.- Member of the Spanish Society of Biochemistry and Molecular Biology since 1996.

4.- Full member of the Spanish Society of Virology since 1996.

5.- Full member of the American Society for Virology since 1996.

6.- Member of the AIDS and Related Research Study Section, NIH, since July 1999.

7.- Ad hoc reviewer of the Experimental Virology Study Section, NIH, February 2002.

7.- Member of the Editorial Board of Virus Research since September 2001.

8.- Member of the Editorial Board of Journal of Virology since January 2002.

9.- Member of the Editorial Board of Virology since January 2002.

10.- Member of the New York Academy of Sciences since January 2002.

8.- **INVITED LECTURES AT MEETINGS AND OTHER INSTITUTIONS**

A. Meetings

1. Vaccines: New Technologies & Applications. Alexandria, VA, USA. March 1994: Preclinical results with a live recombinant vaccine strategy against malaria.

2. Keystone Symposium on Mucosal Immunity. Keystone, CO, USA. January 1995: Genetic engineering of influenza virus for use in vaccination.

3. 14th Japanese Annual Meeting on Influenza. Japanese Alps, Japan. February 1999: Genetically engineered influenza virus vaccines.

4. VI National Congress of Virology. Majadahonda, Spain. October 1999: Attenuation of influenza viruses by reverse genetics techniques.

5. Options for the Control of Influenza IV, Hersonissos, Crete, Greece. September 2000: NS1-mediated inhibition of the type I interferon system during influenza A virus infection.

6. International Symposium on Emmergence and Control of Zoonotic and Paramyxovirus Diseases. Veyrier-du-Lac, France. December 2000: Molecular approaches for influenza virus attenuation and vaccine development.

7. FEBS Practical & Lecture Course "Viral Vectors". German Cancer Research Center (DKFZ), Heidelberg. September 2001: Influenza A viruses as vaccine vectors.

8. Vaccine Immunology Centers Meeting. National Institutes of Health, Bethesda, MD, USA. September 2002: Type I interferon antagonist function of the NS1 protein of influenza virus.

9. Workshop on Engineering RNA Virus Genomes as Biosafe Vectors. Instituto Juan March de Estudios e Investigaciones, Madrid (Spain). October 2002: Plasmid-based reverse genetics for influenza virus.

10. 103rd General Meeting of the American Society for Microbiology. Washington Convention Center, Washington, D.C. May 2003: Antitumor properties of influenza virus vectors.

B. Institutions

1. Center for Molecular Biology, Madrid, Spain. 1995. Expression vectors based on influenza viruses.

2. Institute of Microbiology, University of Salamanca, Salamanca, Spain. 1996. Genetically engineered influenza viruses as vaccine vectors.

3. Institute of Microbiology, University of Agriculture, Vienna, Austria. 1997. Recombinant influenza viruses as vaccine vectors.

4. National Institute of Infectious Diseases, Tokyo, Japan. 1999. The role of interferon in influenza virus pathogenicity.

5. Yamagata University School of Medicine, Yamagata, Japan. 1999. The role of interferon in influenza virus pathogenicity.

6. Kanazawa University School of Medicine, Kanazawa, Japan. 1999. Genetic engineering of influenza viruses.

7. Queens College Biology Department, New York, NY, USA. 1999. Genetic manipulation of influenza viruses: Virus attenuation and viral vectors.

8. Institute for Microbiology & Hygiene, University of Freiburg, Freiburg, Germany. 1999. The

NS1 protein of influenza A virus, a type I interferon antagonist protein.

9. Bio-Méga Research Division, Boehringer Ingelheim, Laval, Québec, Canada. 2000. Viral interferon antagonists as antiviral targets.

10. Shering-Plough Research Institute, Kenilworth, New Jersey, USA. 2000. Viral interferon antagonists as antiviral targets.

11. Research Triangle Park, North Carolina State University, College of Veterinary Medicine, Raleigh, North Carolina, USA. December 2000. Type I interferon antagonist proteins encoded by influenza and Ebola viruses.

12. Centre Européen de Recherches en Virologie et Immunologie, Fondation Mérieux, Lyon, France. December 2000. Type I interferon antagonist proteins encoded by influenza and Ebola viruses.

13. Queens College Biology Department, New York, NY, USA. February 2001. Type I interferon antagonist proteins encoded by influenza and Ebola viruses.

14. Department of Microbiology, University of Salamanca, Salamanca, Spain. April 2001. Inhibiton of the interferon-mediated antiviral responses by influenza and Ebola viruses.

15. Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, Indiana, USA. July 2001. Type I interferon antagonists encoded by influenza and Ebola viruses.

16. Department of Infectious Diseases, Mount Sinai Hospital, New York, New York, USA. September 2001. Type I interferon antagonists encoded by influenza and Ebola viruses.

17. New York Academy of Sciences, New York, New York, USA. January 2002. Molecular design of improved influenza virus vaccines.

18. Department of Microbiology, Washington University, Seattle, Washington, USA. January 2002. Interferon antagonist proteins encoded by influenza and Ebola viruses.

19. Iowa State University, Aims, Iowa, USA. June 2002. Inhibition of the type I interferon system by influenza A viruses.

20. National Animal Disease Center, USDA, Aims, Iowa, USA. June 2002. Reverse genetics approaches for the generation of live vaccines against influenza.

21. Department of Infectious Diseases, Mount Sinai Hospital, New York, New York, USA. November 2002. Evasion of the type I interferon response by influenza viruses.

22. Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis,

Tennessee, USA. December 2002. Evasion of the type I interferon response by influenza viruses.

23. Virology Seminar Series, Columbia University, New York, NY, USA. February 2003. Inhibition of the type I interferon system by negative strand RNA viruses.

24. Division of Nephrology's Research Conferences, Mount Sinai School of Medicine, New York, NY, USA. February 2003. Evasion of type I interferon responses by influenza virus.

25. Department of Microbiology and Immunology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA. February 2003. Virulence factors of influenza A virus: The NS1 protein.

26. Virology Dinner Club, Bristol-Myers Squibb Company, Wallingford, Connecticut, USA. February 2003. Interferon antagonistic properties of the NS1 protein of influenza A virus.

27. Center for Immunology & Microbial Disease, Albany Medical College, Albany, NY, USA. March 2003. Inhibition of the type I interferon system by negative strand RNA viruses.

28. Department of Microbiology, University of Texas Southwestern Medical Center, School of Medicine. April 2003. Evasion of the type I interferon response by negative strand RNA viruses.